Amendments to the Drawings:

Figures 1 through 8 as originally filed have been deleted and Figures 9 through 17 have been renumbered accordingly. No new matter has been added.

Attachment: Replacement sheets (13 pages)
Annotated Marked-up Drawings (37 pages)

REMARKS

Claim Amendments

Claims 1 and 5 have been amended and Claim 7 has been canceled herein. Support for these amendments can be found throughout the specification and in the claims as originally filed. No new matter has been added.

Objections to the Drawings

The drawings have been objected to for containing sequences that are included in the sequence listing. Figures 1 through 8, providing the amino acid sequence and the nucleic acid sequence of various histone deacetylases, have been deleted herein. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-3 and 5 Under 35 U.S.C. §112, First Paragraph

Claims 1-3 and 5 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Office Action states that the specification as filed includes only antisense compounds that hybridize to the human form of histone deacetylase, however, the claims are not limited to the human-isotype specific antisense oligonucleotides as exemplified in the specification. Moreover, the Office Action states that the scope of the antisense compounds of the present invention includes those that hybridize to DNA or RNA of undefined length that "comprises" a region of undefined length of the sequence set forth in SEQ ID NO: 2.

Claim 1 has been amended to recite that the oligonucleotide inhibits the expression of one or more human histone deacetylase isoforms but less than all human histone deacetylase isoforms. The rejection is therefore rendered moot.

Additionally, Applicants disagree that the scope of the antisense compounds of the present invention includes those that hybridize to DNA or RNA of undefined length that "comprises" a region of undefined length of the sequence set forth in SEQ ID NO: 2. As defined in Claim 1, the oligonucleotides are from about 15 to about 26 nucleotides in length and as depicted in the sequence listing, SEQ ID NO 2 is 1611 nucleotides in length. In other words, the claimed oligonucleotides hybridize under physiological conditions to an about 15 nucleotide to about 26 nucleotide region of the 1611 nucleotides of SEQ ID NO 2.

One skilled in the art would clearly understand that Applicants had possession of the full scope of the antisense oligonucleotides encompassed by the instant claims. Reconsideration and withdrawal of the rejection are respectfully requested.

The Office Action also supports the written description rejection with language that appears to state that Applicants have not enabled the instantly claimed invention. Specifically the Office Action states that although the specification teaches the sequences of human histone deacetylase isoforms 1 through 8, a generic search of the term "histone deacetylase" in GenBank resulted in 263 hits for genes encoding a histone deacetylase. Additionally, the Office Action states that effective antisense molecules must be found empirically by screening a large number of candidates for their ability to act inside cells. Applicants will address the comments accordingly.

A generic search for the term "histone deacetylase" in GenBank is a faulty search and although it resulted in 263 "hits", these hits were excessively repetitive and not indicative of 263 different human isoforms of histone deacetylase. To date, only 11 different isoforms of human histone deacetylase are known. However, even if there were 263 different human isoforms of histone deacetylase, Applicants are not required to specifically describe that which is already known. Applicants have provided enough guidance so that one skilled in the art would be able to take the sequence of any known histone deacetylase isoform from any species and come up with an antisense that meets the limitations of the claimed invention. *See* Johns Hopkins Univ. v. Cellpro, Inc., 152 F.3d 1342, 1361 (Fed. Cir. 1998) ; Engel Indus. Inc. v. Lockformer Co., 946 F.2d 1528, 1533 (Fed. Cir. 1991) . ... [T]here is no requirement that the specification enable every mode for making and using the claimed products."; "The reason for such a rule is clear. What would be the value in patenting a composition at all if, by making the slightest alteration in the method of making what is nonetheless the same product, a competitor were able to evade liability? A patent system that permitted such conduct would remove the carrot dangling in front of the inventor's nose. If inventors were so easily divested of their limited monopoly rights attendant to their novel, useful, and nonobvious contributions, they would likely abandon their pursuits and thereby inhibit progress. The law does not permit such an outcome.".

Moreover, even though effective antisense molecules must be found empirically by screening a large number of candidates, this does not necessarily make the experimentation

undue. Applicants respectfully submit that the specification accurately teaches how to practice the claimed invention. One skilled in the art could easily reproduce Applicants' results by simply following the examples and the disclosed oligonucleotides. As to other oligonucleotides, undoubtedly some screening using the methods disclosed in the specification and examples would be required. However, these experiments, which would require no modification of the disclosured assays, would not be undue. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *Massachusetts Institute of Technology v. A.B. Fortia*, 227 U.S.P.Q. 428 (Fed. Cir. 1985). In the antisense field, scientists typically engage in such screening, and would have to do so no matter how many oligonucleotides are exemplified. Applicants have clearly met this requirement.

Rejection of Claims 1-3 and 7 Under 35 U.S.C. §102(e)

Claims 1-3 and 7 are rejected under 35 U.S.C. §102(e) as being anticipated by Besterman et al. (US PAT No 6,953,783).

Claim 7 has been canceled herein, thus rendering the rejection moot as it applies to this claim. Additionally, Claim 1 has been amended to incorporate subject matter from pending Claim 5 thereby obviating this rejection as it applies to Claim 1 (and Claims 2-3 which are dependent on Claim 1). Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-3, 5 and 7 Under 35 U.S.C. §103(a)

Claims 1-3, 5 and 7 are rejected under 35 U.S.C. §103(a) as being unpatentable over Besterman et al. as applied to Claims 1-3 and 7 above, in view of Bennett et al.

The subject matter of Besterman et al. and the instantly claimed invention were, at the time the claimed invention was made, owned by the same person or subject to an obligation of assignment to the same person. Therefore, Besterman et al. does not preclude patentability under this section. The teachings of Bennett et al. do not render the instantly claimed invention obvious. Reconsideration and withdrawal of the invention are respectfully requested.

Provisional Double Patenting

Claims 1-3, 5 and 7 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-11 of copending U.S. Application No. 10/870,587.

As stated by the Examiner, this is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented. If this provisional double patenting rejection is the only remaining rejection in this earlier filed application, Applicants request that the Examiner withdraw the rejection and allow this application to issue as a patent (See MPEP §804(I)(B)). Applicants will then consider filing a Terminal Disclaimer or take any other action deemed necessary in the later filed copending application.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

Dated: October 26, 2006

By _____

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MAQTQGTRRKVCYYYDGDVGNYYYGQGHPMKPHRIRMTHNLLLN

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SGDEDEDDPDKRISICSSDKRIACEEEFSDSEEEGEGGRKNSSNFKKAKRVKTEDEKE

KDPEEKKEVTEEEKTKEEKPEAKGVKEEVKLA (SEQ ID NO:1)

~~FIG. 1A~~ Deleted

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ANNOTATED MARKED-UP DRAWINGS

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 121 cgcagggcac ccggaggaaa gtctgttact actacgacgg ggatgttgga aattactatt
 181 atggacaagg ccacccaatg aagcctcacc gaatccgcat gactcataat ttgctgctca
 241 actatggtct ctaccgaaaa atggaaatct atcgccctca caaagccaat gctgaggaga
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 481 ttaataagca gcagacggac atcgccgtga attgggctgg gggcctgcac catgcaaaga
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 841 tcatgtccaa agtaatggag atgttccagc ctagtgcggt ggtcttacag tgtggctcag
 901 actccctatc tggggatcgg ttaggttgct tcaatctatc tatcaaagga cacgccaagt
 961 gtgtggaatt tgtcaagagc tttaacctgc ctatgctgat gctgggaggc ggtggttaca
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1141 acatcagtcc ttccaatatg actaaccaga acacgaatga gtacctggag aagatcaaac
1201 agcgactgtt tgagaacctt agaatgctgc cgcacgcacc tggggtccaa acgcaggcga
1261 ttcctgagga cgccatccct gaggagagtg gcgatgagga cgaagacgac cctgacaagc
1321 gcatctcgat ctgctcctct gacaaacgaa ttgcctgtga ggaagagttc tccgattctg
1381 aagaggaggg agaggggggc cgcaagaact cttccaactt caaaaaagcc aagagagtca
1441 aaacagagga tgaaaaagag aaagacccag aggagaagaa aggaatcacc gaagaggaga
1501 aaaccaagga ggagaagcca gaagccaaag gggtcaagga ggaggccaag ttggcctgaa
1561 tggacctctc cagctctggc ttcctgctga gtccctcacg tttctttccc c (SEQ ID NO:2)
```

FIG. 1B

Deleted

2/37

ANNOTATED MARKED-UP DRAWINGS

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AFDGLFEFCQLSTGGSVAGAVKLNRQQTDMAVNWAGGLHHAKKYEASGFCYVNDIVLA

ILELLKYHQRVLYIDIDIHHRGDGVEEAFYTTDRVMTVSFYGEYFPGTGDLRDIGAG

KGKYYAVNFPMCDGIDDESYGQIFKPIISKVMEMYQPSAVVLQCGADSLSGDRLGCFN

LTVKGHAKCVEVVKTFNLPLLMLGGGGYTILRNVARCWTYETAVALDCEIPNELPYNDY

FEYFGPDFKLHISPSNMTNQNTPEYMEKIKQRLFENLRMLPHAPGVQMQAIPEDAVHE

DSGDEDGEDPDKRISIRASDKRIACDEEFSDSEDEGEGGRNVADHKKGAKARIEED

KKETEDKKTDVKEEDKSKDNSGEKTDTKGTKSEQLSNP (SEQ ID NO:3)

FIG. 2A

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ANNOTATED MARKED-UP DRAWINGS

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 301 cctcatagaa tccgcatgac ccataacttg ctgttaaatt atggcttaca cagaaaaatg
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 541 ctctcaactg gcggttcagt tgctggagct gtgaagttaa accgacaaca gactgatatg
 601 gctgttaatt gggctggagg attacatcat gctaagaaat acgaagcatc aggatcctgt
 661 tacgttaatg atattgtgct tgccatcctt gaattactaa agtatcatca gagagtctta
 721 tatatcgata tagatattca tcatggtgat ggtgtcgaag aagcttttta tacaacagat
 781 cgtgtaatga cggtatcatt ccataaatat ggggaatact ttcctggcac aggagacttg
 841 agggatattg gtgctggaaa aggcaaatac tatgctgtca attttccaat gtgtgatggt
 901 atagacgatg agtcatatgg gcagatattt aagcctatta tctcaaaggt gatggagatg
 961 tatcaaccta gtgctgtggt attacagtgt ggtgcagact cattatctgg tgatagactg
1021 ggttgtttca atctaacagt caaaggtcat gctaaatgtg tagaagttgt aaaaactttt
1081 aacttaccat tactgatgct tggaggaggt ggctacacaa tccgtaatgt tgctcgatgt
1141 tggacatatg agactgcagt tgcccttgat tgtgagattc ccaacgagtt gccatataat
1201 gattactttg agtattttgg accagacttc aaactgcata ttagtccttc aaacatgaca
1261 aaccagaaca ctccagaata tacggaaaag ataaaacagc gtttgtttga aaatttgcgc
1321 atgttacctc atgcacctgg tgtccagatg caagctattc cagaagatgc tgttcatgaa
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ANNOTATED MARKED-UP DRAWINGS

FIG. 2B

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MIVFKPYQASQHDMCRFHSEDYIDFLQRVSPTNMQGFTKSLNAPNVGDDCPVFPGLFE

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FIG. 3A DELETED

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ANNOTATED MARKED-UP DRAWINGS

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 241 ctccgaggac tacattgact tcctgcagag agtcagcccc accaatatgc aaggcttcac
 301 caagagtctt aatgccttca acgtaggcga tgactgccca gtgtttcccg ggctctttga
 361 gttctgctcg cgttacacag gcgcatctct gcaaggagca acccagctga acaacaagat
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 481 tggcttctgc tatgtcaacg acattgtgat tggcatcctg gagctgctca agtaccaccc
 541 tcgggtgctc tacattgaca ttgacatcca ccatggtgac ggggttcaag aagctttcta
 601 cctcactgac cgggtcatga cggtgtcctt ccacaaatac ggaaattact tcttccctgg
 661 cacaggtgac atgtatgaag tcggggcaga gagtgggccgc tactactgtc tgaacgtgcc
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1261 gaactatagc aggccaggagg catccaatga gttctatgat ggagaccatg acaatgacaa
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1921 atttttttgta cctttgatgg tttagcggcc gcgc (SEQ ID NO:6)
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FIG. 3B

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ANNOTATED MARKED-UP DRAWINGS

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GGHDLTAICDASEACVSALLGNELDPLPEKVLQQRPNANAVRSMEKVMEIHSKYWRCL

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DELETED

FIG. 4A

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ANNOTATED MARKED-UP DRAWINGS

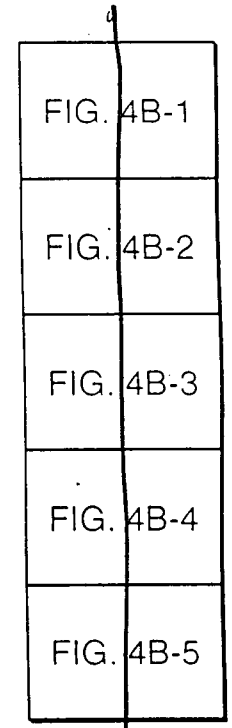

FIG. 4B

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FIG. 4B-1

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ANNOTATED MARKED-UP DRAWINGS

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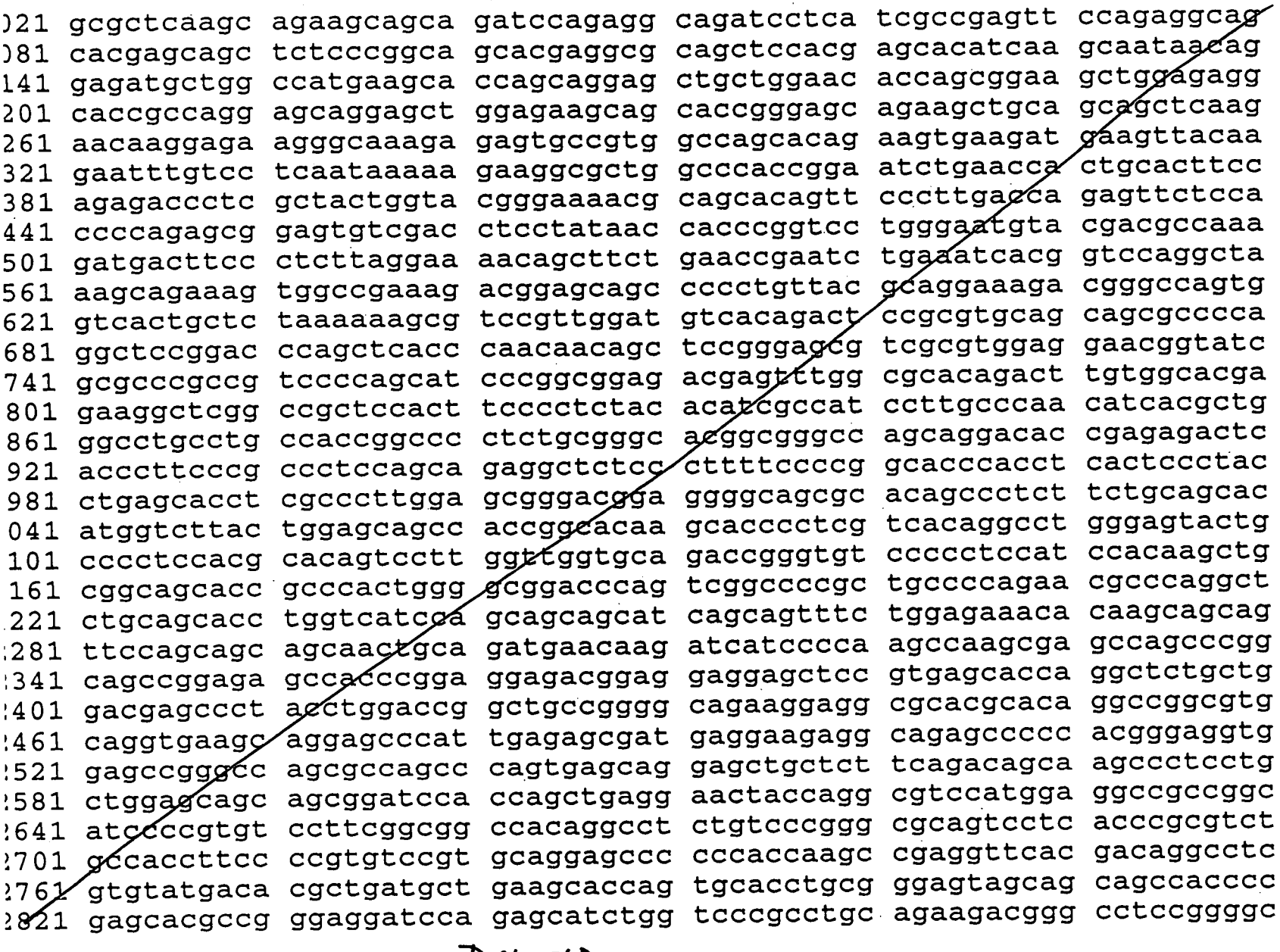

FIG. 4B-2

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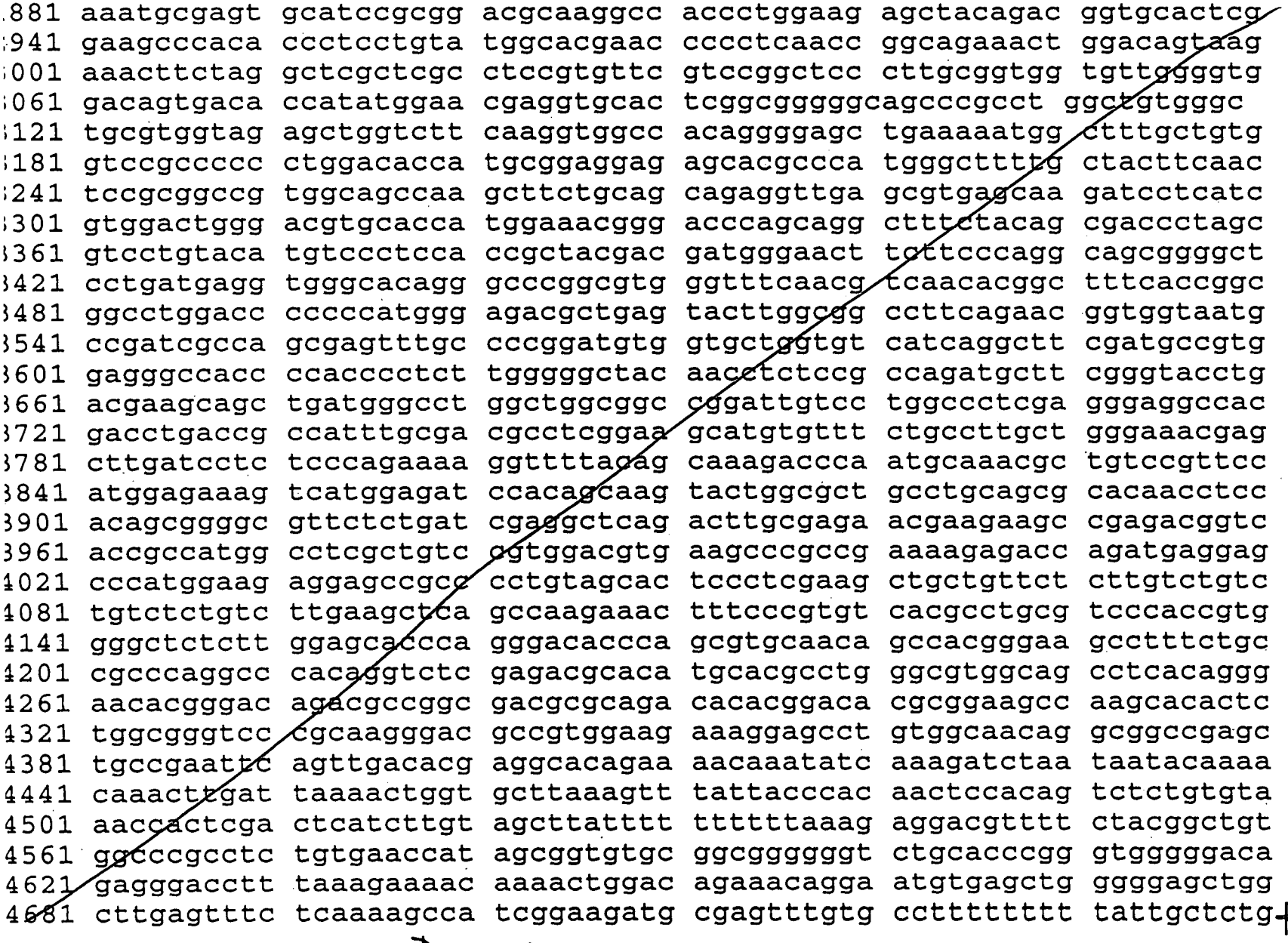
ANNOTATED MARKED-UP DRAWINGS



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~~FIG. 4B-3~~

~~10/37~~

ANNOTATED MARKED-UP DRAWINGS

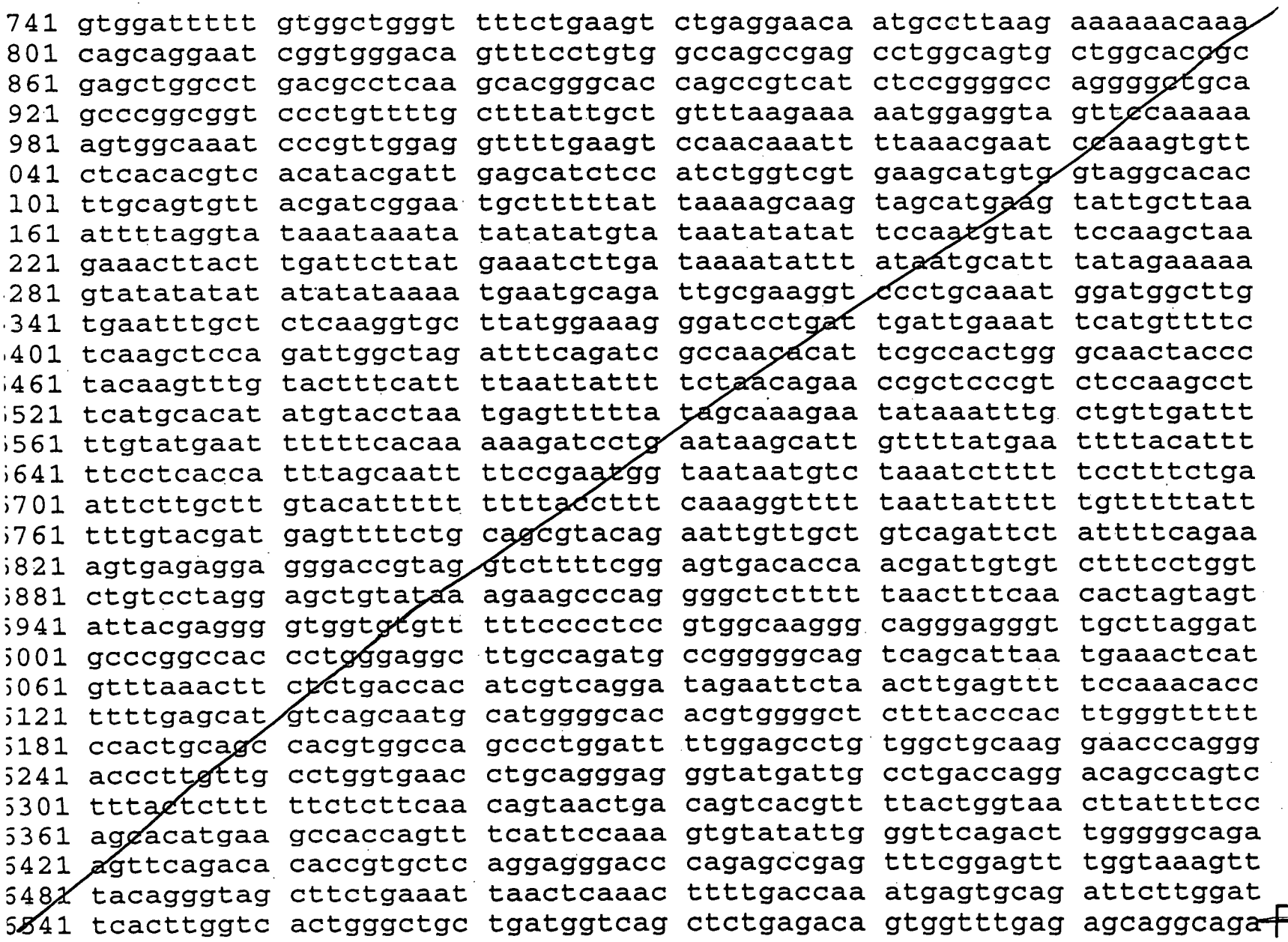

FIG. 4B-4

DELETED

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ANNOTATED MARKED-UP DRAWINGS

601 acggtcttgg gacttgtttg actttcccct ccctggtggc cactctttgc tctgaagccc
661 agattggcaa gaggagctgg tccattcccc attcatggca cagaacagtg gcagggccca
721 gctagcaggc tcttctggcc tccttggcct cattctctgc atagccctct ggggatcctg
781 ccacctgccc tcttaccccg ccgtggctta tggggaggaa tgcatcatct cactttttt
841 ttttaagcag atgatgggat aacatggact gctcagtggc caggttatca gtgggggac
901 ttaattctaa tctcattcaa atggagacga cctctgcaaa ggcctggcag ggggaggcaa
961 gtttcatctg tcagctcact ccagcttcac aaatgtgctg agagcattac tgtgtagcct
021 tttctttgaa gacacactcg gctcttctcc acagcaagcg tccagggcag atggcagagg
081 atctgcctcg gcgtctgcag gcgggaccac gtcagggagg gttccttcat gtgttctccc
141 tgtgggtcct tggaccttta gccttttttct tcctttgcaa aggccttggg ggcactggct
201 gggagtcagc aagcgagcac tttatatccc tttgagggaa accctgatga cgccactggg
261 cctcttggcg tctgacctgc cctcgccgct tcccgccgtg ccgcagcgtg cccacgtgcc
321 cacgccccac cagcaggcgg ctgccccgga ggccgtggcc cgctgggact ggccgccccct
381 ccccagcgtc ccagggctct ggttctggag ggccactttg tcaaggtgtt tcagtttttc
441 tttacttctt ttgaaaatct gtttgcaagg ggaaggacca tttcgtaatg gtctgacaca
501 aaagcaagtt tgatttttgc agcactagca atggactttg ttgcttttct ttttgatcag
561 aacattcctt ctttactggt cacagccacg tgctcattcc attcttcttt ttgtagactt
621 tgggcccacg tgttttatgg gcattgatac atatataaat atatagatat aaatatatat
681 gaatacattt ttttaagttt cctacacctg gaggttgcat ggactgtacg accggcatga
741 ctttatattg tatacagatt ttgcacgcca aactcggcag ctttggggaa gaagaaaaat
801 gcctttctgt tcccctctca tgacatttgc agatacaaaa gatggaaatt tttctgtaaa
861 acaaaacctt gaaggagagg agggcgggga agtttgcgtc ttattgaact tattcttaag
921 aaattgtact ttttattgta agaaaaataa aaaggactac ttaaacattt gtcatattaa
981 gaaaaaaagt ttatctagca cttgtgacat accaataata gagtttattg tatttatgtg
041 gaaacagtgt tttagggaaa ctactcagaa ttcacagtga actgcctgtc tctctcgagt
101 tgatttggag gaatttgtt ttgttttgtt ttgtttgttt ccttttatct ccttccacgg
161 gccaggcgag cgccgcccgc cctcactggc cttgtgacgg tttattctga ttgagaactg
221 ggcggactcg aaagagtccc cttttccgca cagctgtgtt gacttttaa ttacttttag
281 gtgatgtatg gctaagattt cactttaagc agtcgtgaac tgtgcgagca ctgtggttta
341 caattatact ttgcatcgaa aggaaaccat ttcttcattg taacgaagct gagcgtgttc
401 ttagctcggc ctcactttgt ctctggcatt gattaaaagt ctgctattga aagaaaaag (SEQ ID NO:8)

FIG. 4B-5

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DELETED

ANNOTATED MARKED-UP DRAWINGS

LRQGGTLTGKFMSTSSIPGCLLGVALEGDGSPHGHASLLQHVLL

LEQARQQSTLIAVPLHGQSPLVTGERVATSMRTVGKLPRHRPLSRTQSSPLPQSPQAL

QQLVMQQQHQQFLEKQKQQQLQLGKILTKTGELPRQPTTHPEETEEELTEQQEVLLGE

GALTMPREGSTESESTQEDLEEEDEEEDGEEEDCIQVKDEEGESGAEEGPDLEEPGA

GYKKLFSDAQPLQPLQVYQAPLSLATVPHQALGRTQSSPAAPGGMKSPPDQPVKHLFT

TGVVYDTFMLKHQCMCGNTHVHPEHAGRIQSIWSRLQETGLLSKCERIRGRKATLDEI

QTVHSEYIHTLLYGTSPLNRQKLDSKKLLGPISQKMYAVLPCGGIGVDSDTVWNEMHSS

SAVRMAVGCLLELAFKVAAGELKNGFAIIRPPGHHAEESTAMGFCFFNSVAITAKLLQ

QKLNVGKVLIVDWDIHHGNGTQQAFYNDPSVLYISLHRYDNGNFFPGSGAPEEVGGGP

GVGYNVNVAWTGGVDPPIGDVEYLTAFRTVVMPIAHEFSPDVVTLVSAGFDAVEGHLSP

LGGYSVTARCFGHLTRQLMTLAGGRVVLALEGGHDLTAICDASEACVSALLSVELQPL

DELVLQQKPNINAVATLEKVIETQSKHWSCVQKFAAGLGRSLREAQAGETEEAETVSA

MALLSVGAEQAQAAAAREHSPRPAEEPMEQEPAL (SEQ ID NO:9)

DELETED

FIG. 5A

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ANNOTATED MARKED-UP DRAWINGS

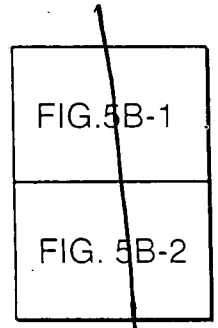

FIG. 5B

```
   1 ccctgcggca gggtggcacg ctgaccggca agttcatgag cacatcctct attcctggct
  61 gcctgctggg cgtggcactg gagggcgacg ggagccccca cgggcatgcc tcctgctgtc
 121 agcatgtgct gttgctggag caggcccggc agcagagcac cctcattgct gtgccactcc
 181 acgggcagtc cccactagtg acgggtgaac gtgtggccac cagcatgcgg acggtaggca
 241 agctcccgcg gcatcggccc ctgagccgca ctcagtcctc accgctgccg cagagtcccc
 301 aggccctgca gcagctggtc atgcaacaac agcaccagca gttcctggag aagcagaagc
 361 agcagcagct acagctgggc aagatcctca ccaagacagg ggagctgccc aggcagccca
 421 ccacccaccc tgaggagaca gaggaggagc tgacggagca gcaggaggtc ttgctggggg
 481 agggagccct gaccatgccc cgggagggct ccacagagag tgagagcaca caggaagacc
 541 tggaggagga ggacgaggaa gaggatgggg aggaggagga ggattgcatc caggttaagg
 601 acgaggaggg cgaggagtggt gctgaggagg ggcccgactt ggaggagcct ggtgctggat
 661 acaaaaaact gttctcagat gcccagccgc tgcagccttt gcaggtgtac caggcgcccc
 721 tcagcctggc cactgtgccc caccaggccc tgggccgtac ccagtcctcc cctgctgccc
 781 ctgggggcat gaagagcccc ccagaccagc ccgtcaagca cctcttcacc acaggtgtgg
 841 tctacgacac gttcatgcta aagcaccagt gcatgtgcgg gaacacacac gtgcaccctg
```

FIG. 5B-1

DELETED

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ANNOTATED MARKED-UP DRAWINGS

```
 901 agcatgctgg ccggatccag agcatctggt cccggctgca ggagacaggc ctgcttagca
 961 agtgcgagcg gatccgaggt cgcaaagcca cgctagatga gatccagaca gtgcactctg
1021 aataccacac cctgctctac gggaccagtc ccctcaaccg gcagaagcta gacagcaaga
1081 agttgctcgg ccccatcagc cagaagatgt atgctgtgct gccttgtggg ggcatcgggg
1141 tggacagtga caccgtgtgg aatgagatgc actcctccag tgctgtgcgt atggcagtgg
1201 gctgcctgct ggagctggcc ttcaaggtgg ctgcaggaga gctcaagaat ggatttgcca
1261 tcatccggcc cccaggacac cacgccgagg aatccacagc cacgggattc tgcttcttca
1321 actctgtagc catcaccgca aaactcctac agcagaagtt gaacgtgggc aaggtcctca
1381 tcgtggactg ggacattcac catggcaatg gcacccagca ggcgttctat aatgacccct
1441 ctgtgctcta catctctctg catcgctatg acaacgggaa cttctttcca ggctctgggg
1501 ctcctgaaga ggttggtgga ggaccaggcg tggggtacaa tgtgaacgtg gcatggacag
1561 gaggtgtgga ccccccccatt ggagacgtgg agtaccttac agccttcagg acagtggtga
1621 tgcccattgc ccacgagttc tcacctgatg tggtcctagt ctccgccggg tttgatgctg
1681 ttgaaggaca tctgtctcct ctgggtggct actctgtcac cgccagatgt tttggccact
1741 tgaccaggca gctgatgacc ctggcagggg gccgggtggt gctggccctg gagggaggcc
1801 atgacttgac cgccatctgt gatgcctctg aggcttgtgt ctcggctctg ctcagtgtag
1861 agctgcagcc cttggatgag gcagtcttgc agcaaaagcc caacatcaac gcagtggcca
1921 cgctagagaa agtcatcgag atccagagca aacactggag ctgtgtgcag aagttcgccg
1981 ctggtctggg ccggtccctg cgagaggccc aagcaggtga ggccgaggag gccgagactg
2041 tgagcgccat ggccttgctg tcggtggggg ccgagcaggc ccaggctgcg gcagcccggg
2101 aacacagccc caggccggca gaggagccca tggagcagga gcctgccctg tgacgccccg
2161 gccccccatcc ctctcggctt caccattgtg attttgttta ttttttctat taaaaacaaa
2221 aagtcacaca ttc (SEQ ID NO:10)
```

FIG. 5B-2 DELETED

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ANNOTATED MARKED-UP DRAWINGS

```
   1 mtstgqdstt trqrrsrqnp qsppqdssvt skrnikkgav prsipnlaev kkkgkmkklg
  61 qameedlivg lqgmdlnlea ealagtglvl deqlnefhcl wddsfpegpe rlhaikeqli
 121 qeglldrcvs fqarfaekee lmlvhsleyi dlmettqymn egelrvladt ydsvylhpns
 181 yscaclasgs vlrlvdavlg aeirngmaii rppghhaqhs lmdgycmfnh vavaaryaqq
 241 khrirrvliv dwdvhhgqgt qftfdqdpsv lyfsihryeq grfwphlkas nwsttgfgqg
 301 qgytinvpwn qvgmrdadyi aaflhvllpv alefqpqlvl vaagfdalqg dpkgemaatp
 361 agfaqlthll mglaggklil sleggynira laegvsaslh ellgdpcpml espgapcrsa
 421 qasvscalea lepfwevlvr stetverdnm eednveesee egpweppvlp iltwpvlqsr
 481 tglvydqnmm nhcnlwdshh pevpqrilri morleelgia grcltitprp ateaelltch
 541 saeyvghlra tekmktrelh ressnfdsiy icpstfacaq Iatgaacrlv eavisgevin
 601 gaavvrppgh haeqdaacgf cffnsvavaa rhaqtisgha lrilivdwdv hhgngtqhmf
 661 eddpsvlyvs lhrydhgtff pmgdeeassq igraagtgft vnvawngprm gdadylaawh
 721 rlvlpiayef npelvlvsag fdaargdplg gcqvspegya hlthllmgla sgriilileg
 781 gynltsises maactrsilg dpppllt1pr pplsgalasi tetiqvhrry wrslrvmkve
 841 dregpssskl vtkkapqppak prlaermttr ekkvleagmg kvtsasfgee stpgqtnset
 901 avvalcqdqp seaatggatl aqtiseaaig gamlgqttse eavggatpdq ttseetvgga
 961 ildqttseda vggatigqtt seeavggatl aqtiseaame gatldqttse eapggteliq
1021 tplasstdhq tpptspvqgt tpqispstli gslrtlelgs esqgasesqa pgeenllgea
1081 agggdmadsm lmqgsrgltd qaifyavtpl pwcphlvavc pipaagldvt qpcgdcgtiq
1141 enwvclscyq vycgryingh mlqhhgnsgh plvlsyidls awcyycqayv hhqalldvkn
1201 iahqnkfged mphph (SEQ ID:11)
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FIG. 6A DELETED

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ANNOTATED MARKED-UP DRAWINGS

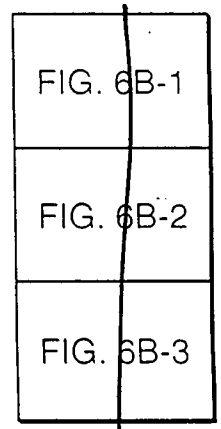

FIG. 6B

```
  1 gggcagtccc ctgaggagcg gggctggttg aaacgctagg ggcgggatct ggcggagtgg
 61 aagaaccgcg gcaggggcca agcctcctca actatgacct caaccggcca ggattccacc
121 acaaccaggc agcgaagaag taggcagaac ccccagtcgc cccctcagga ctccagtgtc
181 acttcgaagc gaaatattaa aaagggagcc gttccccgct ctatccccaa tctagcggag
241 gtaaagaaga aaggcaaaat gaagaagctc ggccaagcaa tggaagaaga cctaatcgtg
301 ggactgcaag ggatggatct gaacctcgag gctgaagcac tggctggcac tggcttggtg
361 ttggatgagc agttaaatga attccattgc ctctgggatg acagcttccc ggaaggccct
421 gagcggctcc atgccatcaa ggagcaactg atccaggagg gcctcctaga tcgctgcgtg
481 tcctttcagg cccggtttgc tgaaaaggaa gagctgatgt tggttcacag cctagaatat
```

FIG. 6B-1 DELETED

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DELETED

FIG. 6B-2

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ANNOTATED MARKED-UP DRAWINGS

341 gggggctgcc aggtgtcacc tgagggttat gcccacctca cccacctgct gatgggcctt
401 gccagtggcc gcattatcct tatcctagag ggtggctata acctgacatc catctcagag
461 tccatggctg cctgcactcg ctccctcctt ggagacccac cacccCtgct gaccctgcca
521 cggcccccac tatcaggggc cctggcctca atcactgaga ccatccaagt ccatcgcaga
581 tactggcgca gcttacgggt catgaaggca gaagacagag aaggaccctc cagttctaag
641 ttggtcacca agaaggcacc ccaaccagcc aaacctaggt tagctgagcg gatgaccaca
701 cgagaaaaga aggttctgga agcaggcatg gggaaagtca cctcggcatc atttggggaa
761 gagtccactc caggccagac taactcagag acagctgtgg tggccctcac tcaggaccag
821 ccctcagagg cagccacagg gggagccact ctggcccaga ccatttctga ggcagccatt
881 gggggagcca tgctgggcca gaccacctca gaggaggctg tcgggggagc cactccggac
941 cagaccacct cagaggagac tgtgggagga gccattctgg accagaccac ctcagaggat
001 gctgttgggg gagccacgct gggccagact acctcagagg aggctgtagg aggagctaca
061 ctggcccaga ccatctcgga ggcagccatg gaggggagcca cactggacca gactacgtca
121 gaggaggctc caggggggcac cgagctgatc caaactcctc tagcctcgag cacagaccac
181 cagacccccc caacctcacc tgtgcaggga actacacccc agatatctcc cagtacactg
241 attgggagtc tcaggacctt ggagctaggc agcgaacctC agggggcctc agaatctcag
301 gccccaggag aggagaacct accaggagag gcagctggag gtcaggacat ggctgattcg
361 atgctgacgc agggatctag gggcctcact gatcaggcca tattttatgc tgtgacacca
421 ctgccctggt gtccccattc ggtggcagta tgccccatac ctgcagcagg cctagacgtg
481 acccaacctt gtggggactg tggaacaatc caagagaact gggtgtgtct ctcttgctat
541 caggtctacc gtggtcgtta catcaatggc cacatgctcc aacaccatgg aaattctgga
601 cacccgctgg tcctcagcca catcgacctg tcagcctggc gttactactg tcaggcctat
661 gtccaccacc aggctctcct agatgtgaag aacatcgccc accagaacaa gtttggggag
721 gatatgcccc acccacacta agccccagaa tacggtccct cttcaccttc tgaggcccac
781 gatagaccag ttccagcctg ttccaggctg taccttggat gaggggtagc ctcccactgc
841 atcccatcct gaatatcctt tgcaactccc caagagtgct tatttaagtg ttaatacttt
901 taagagaact gcgacgatta attgtggatc tccccctgcc catcgcccgc ttgaggggca
961 ccactactcc agcccagaag gaaaggggggg cagctcagtg gccccaagag ggagccgata
021 tcatgaggat aacattggcg ggaggggagt taactggcag gcatggcaag gttgcatatg
081 taataaagta caagctgtt (SEQ ID NO: 12)

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ANNOTATED MARKED-UP DRAWINGS

DELETED

FIG. 6B-3

```
  1 mdlrvgqrpp vepppeptll alqrpqrlhh hlflaglqqq rsvepmrlsm dtpmpelqvg
 61 pqeqelrqll hkdkskrsav assvvkqkla evilkkqqaa lertvhpnsp gipyrtlepi
121 etegatrsml ssflppvpsi psdppehfpl rktvsepnlk lrykpkksle rrknpllrke
181 sappslrrrp aetlgdssps ssstpasgcs spndsehgpn pilgdsdrrt hptlgprgpi
241 lgsphtplfl phglepeagg clpsrlqpil lldpsgshap lltvpglgpl pfhfaqsimt
301 terlsgsglh wplsrtrsep lppsatappp pgpmaprleq lkthvqvikr sakpsekprl
361 rqipsaedle tdgggpgqvv ddglehrelg hgqpeargpa plqqhpqvii weqqrlagrl
421 prgstgdcvi lplaqgghrp lsraqsspaa pasisapepa sqarvlssse tpartlpflt
481 gliydsvmlk hqcscgdnsr hpehagriqs iwsrlqergl rsqceclrgr kasieelqsv
541 hserhvllyg tnplsrlkld ngklagiiaq rmfemlpcgg vgvdtdtiwn elhssnaarw
601 aagsvtdlaf kvasrelkng favvrppghh adhstamgfc ffnsvaiacr qlqqqskask
661 askilivdwd vhhgngtqqt fyqdpsvlyi slhrhddgnf fpgsgavdev gagsgegfnv
721 nvawaggldp pmgdpeylaa frivvmpiar efspdlvlvs agfdaaeghp aplggyhvsa
781 kcfgymtqql mnlaggavvl alegghdlta icdaseacva allgnrvdpl seegwkqkpq
841 pqchplsggr dpgaq (SEQ ID NO:13)
```

~~FIG. 7A~~ DELETED

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ANNOTATED MARKED-UP DRAWINGS

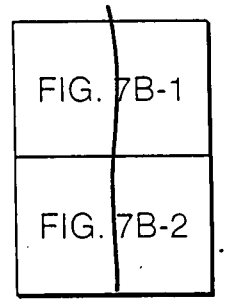

FIG. 7B

```
   1 ataataccta ccttgcagga ccacgacagg attaagtgag gaaaaacccc catgagagtg
  61 ttttgccatt gtcaagtgag cctgagggag gctgaggggg gatcaggctg tatcatgccc
 121 ccgaggacaa actttccagt ttaccctgct ccctctctct gtccctaggc tgccccaggc
 181 cctgcgcaga cacaccaggc cctcagccgc agcccatgga cctgcgggtg ggccagcggc
 241 ccccagtgga gcccccacca gagcccacat tgctggccct gcagcgtccc cagcgcctgc
 301 accaccacct cttcctagca ggcctgcagc agcagcgctc ggtggagccc atgaggctct
 361 ccatggacac gccgacgccc gagttgcagg tgggacccca ggaacaagag ctgcggcagc
 421 ttctccacaa ggacaagagc aagcgaagtg ctgtagccag cagcgtggtc aagcagaagc
 481 tagcggaggt gattctgaaa aaacagcagg cggccctaga aagaacagtc catcccaaca
 541 gccccggcat tccctacaga accccggagc ccctggagac ggaaggagcc acccgctcca
 601 tgctcagcag ccttccgcct cctgctccca gcccgcccag tgacccccca gagcactccc
 661 ctctgcgcaa gacagtctct gagcccaacc tgaagctgcg ccataagccc aagaagtccc
 721 cggagcggag gaagaatcca ctgctccgaa aggagagtgc gccccccagc ccccggcggc
 781 ggcccgcaga gaccctcgga gactcctccc caagtagtag cagcacgccc gcatcagggt
 841 gcagtccccc caatgacagc gagcacggcc ccaatcccat cctgggcgac agtgaccgca
 901 ggacccatcc gactctgggc ccccgggggc caatcctggg gagcccccac actcccctct
 961 tcctgcccca tggcttggag cccgaggctg ggggcacctt gccctcccgc ctgcagccca
1021 ttcctctcct ggacccctca ggctctcatg ccccgctgct gactgtgccc gggcttgggc
1081 ccttgccctt ccactttgcc cagtccttaa tgaccaccga gcggctctct gggtcaggcc
1141 tccactggcc actgagccgg actcgctcag agcccctgcc ccccagtgcc accgctcccc
1201 caccgccggg ccccatgcag ccccgcctgg agcagctcaa aactcacgtc caggtgatca
1261 agaggtcagc caagccgagt gagaagcccc ggctgcggca gataccctcg gctgaagacc
1321 tggagacaga tggcgggggа ccgggccagg tggtggacga cggcccggag cacagggagc
```

FIG. 7B-1

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DELETED

ANNOTATED MARKED-UP DRAWINGS

3381 tgggccatgg gcagcccgag gccagaggcc ccgctcctct ccagcagcac cctcaggtgt
3441 tgctctggga acagcagcga ctggctgggc ggctcccccg gggcagcacc ggggacactg
3501 tgctgcttcc tctggcccag ggtgggcacc ggcctctgtc ccgggctcag tcttccccag
3561 ccgcacctgc ctcactgtca gccccagagc ctgccagcca ggcccgagtc ctctccagct
3621 cagagacccc tgccaggacc ctgcccttca ccacagggct gatctatgac tcggtcatgc
3681 tgaagcacca gtgctcctgc ggtgacaaca gcaggcaccc ggagcacgcc ggccgcatcc
3741 agagcatctg gtcccggctg caggagcggg ggcctcggag ccagtgtgag tgtctccgag
3801 gccggaaggc ctccctggaa gagctgcagt cggtccactc tgagcggcac gtgctcctct
3861 acggcaccaa cccgctcagc cgcctcaaac tggacaacgg gaagctggca gggctcctgg
3921 cacagcggat gtttgagatg ctgccctgtg gtggggttgg ggtggacact gacaccatct
3981 ggaatgagct tcattccLcc aatgcagccc gctgggccgc tggcagtgtc actgacctcg
4041 ccttcaaagt ggcttctcgt gagctaaaga atggtttcgc tgtggtgcgg cccccaggac
4101 accatgcaga tcattcaaca gccatgggct tctgcttctt caactcagtg gccatcgcct
4161 gccggcagct gcaacagcag agcaaggcca gcaaggccag caagatcctc attgtagact
4221 gggacgtgca ccatggcaac ggcacccagc aaaccttcta ccaagacccc agtgtgctct
4281 acatctccct gcatcgccat gacgacggca acttcttccc ggggagtggg gctgtggatg
4341 aggtaggggc tggcagcggt gagggcttca atgtcaatgt ggcctgggct ggaggtctgg
4401 acccccccat gggggatcct gagtacctgg ctgctttcag gatagtcgtg acgcccatcg
4461 cccgagagtt ctctccagac ctagtcctgg tgtctgccgg atttgatgct gctgagggtc
4521 acccggcccc acLgggtggc taccatgttt ctgccaaatg ttttggatac atgacgcagc
4581 aactgatgaa cctggcagga ggcgcagtgg tgctggcctt ggagggtggc catgacctca
4641 cagccatctg tgacgcctct gaggcctgtg tggctgctct tctgggtaac agggtggatc
4701 ccctttcaga agaaggctgg aaacagaaac cccaacctca atgccactcg ctctctggag
4761 gccgtgatcc gggtgcacag taaatactgg ggctgcatgc agcgcctggc ctcctgtcca
4821 gactcctggg tgcctagagt gccaggggct gacaaagaag aagtggaggc agtgaccgca
4881 ctggcgtccc tctctgtggg catcctggct gaagataggc cctcggagca gctggtggag
4941 gaggaagaac ctatgaatct ctaaggctct ggaaccatct gcccgcccac catgcccttg
5001 ggacctggtt ctcttctaac ccctggcaat agcccccatt cctgggtctt tagagatcct
5061 gtgggcaagt agttggaacc agagaacagc ctgcctgctt tgacagttat cccagggagc
5121 gtgagaaaat c (SEQ ID NO:14)

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ANNOTATED MARKED-UP DRAWINGS

DELETED

FIG. 7B-2

```
  1 meepeepads gqslvpvyiy speyvsmcds lakipkrasm vhslieayal hkqmrivkpk
 61 vasmeematf htdaylqhlq kvsqegdddh pdeieyglgy dcpategifd yaaaiggati
121 taaqclidgm ckvainwsgg whhakkdeas gfcylndavl gilrlrrkfe rilyvdldlh
181 hgdgvvedafs ftskvmtevsl hkfspgffpg tgdvsdvglg kgryysvnvp iqdgiqdeky
241 yqicesvlke vyqafnpkav vlqlgadtia gdpmcsfnmt pvgigkclky ilqwqlatli
301 lgggynlan tarcwtyltg vilgktlsse ipdbefftay gpdyvleitp scrpdrneph
361 riqqilnyik gnlkhvv (SEQ ID NO:15)
```

FIG. 8A DELETED

```
   1 gaaattcggc acgagctcgt gccgaattcg gcacgagaac ggttttaagc ggaagatgga
  61 ggagccggag gaaccggcgg acagtgggca gtcgctggtc ccggtttata tctatagtcc
 121 cgagtatgtc agtatgtgtg actccctggc caagatcccc aaacgggcca gtatggtgca
 181 ttctttgatt gaagcatatg cactgcataa gcaaatgagg atagttaagc ctaaagtggc
 241 ctccatggag gagatggcca ccttccacac tgatgcttat ctgcagcatc tccagaaggt
 301 cagccaagag ggcgatgatg atcatccgga ctccatagaa tatgggctag gttatgactg
 361 cccagccact gaagggatat ttgactatgc agcagctata ggaggggcta cgatcacagc
 421 tgcccaatgc ctgattgacg gaatgtgcaa agtagcaatc aactggtctg gagggtggca
 481 tcatgcaaag aaagatgaag catctggttt tcgttatctc aatgatgctg tcctgggaat
 541 attacgattg cgacggaaat ttgagcgtat tccctacgtg gattcggatc tgcaccatgg
 601 agatggtgta gaagacgcat tcagtttcac ctccaaagtc atgaccgtgt ccctgcacaa
 661 attctcccca ggatttttcc caggaacagg tgacgtgtcc gacgttggcc tagggaaggg
 721 acggtactac agtgtaaatg tgcccatcca ggatggcata caagatgaaa aatattacca
 781 gatctgcgaa agtgtactaa aggaagtata ccaagccttt aatcccaaag cagtggtctt
 841 acagctggga gccgacacaa tagctgggga tcccatgtgc tcctttaaca tgactccagt
 901 gggaattggc aagtgtctca agtacatccc tcaatggcag ttggcaacac tcatttcggg
 961 aggaggaggc tataaccttg ccaacacggc tcgatgctgg acatacttga ccggggtcat
1021 cctagggaaa acactatcct ctgagatccc agatcatgag tttttcacag catatggtcc
1081 tgattatgtg ctggaaatca cgccaagctg ccggccagac cgcaatgagc cccaccgaat
1141 ccaacaaatc ctcaactaca tcaaagggaa tctgaagcat gtggtctagt tgacagaaag
1201 agatcaggtt tccagagctg aggagtggtg cctataatga agacagcgtg tttatgcaag
1261 cagtttgrgg aatttgtgac tgcagggaaa atttgaaaga aattacttcc tgaaaatttc
1321 caaggggcat caagtggcag ctggcttcct ggggtgaaga ggcaggcacc ccagagtcct
1381 caactggacc taggggaaga aggagatarc ccacatttaa agttcttatt taaaaaaaca
1441 cacacacaca aatgaaattt ttaatctttg aaaattattt ttaagcgaat tggggagggg
1501 agtattttaa tcatcttaaa tgaaacagat cagaagctgg atgagagcag tcaccagttt
1561 gtagggcagg aggcagctga caggcagggn tngggcctcn ggaccancca ngtggagccc
1621 tgggagagan ggtactgatc ngcagactgg gagg (SEQ ID NO:16)
```

FIG. 8B

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ANNOTATED MARKED-UP DRAWINGS

ANNOTATED MARKED-UP DRAWINGS

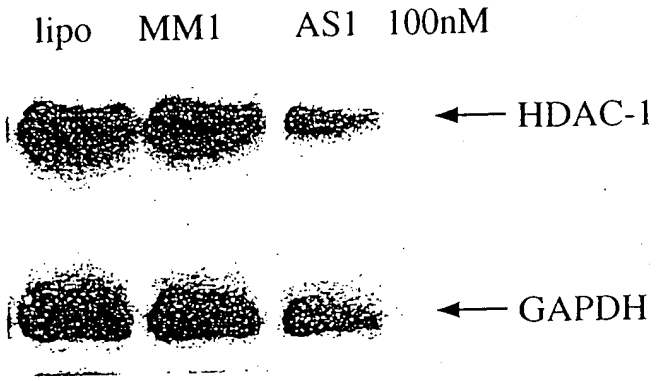


FIG. ~~9A~~ 1A

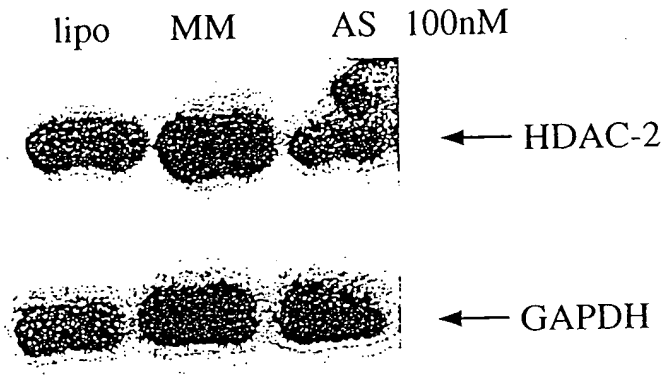


FIG. ~~9B~~ 1B

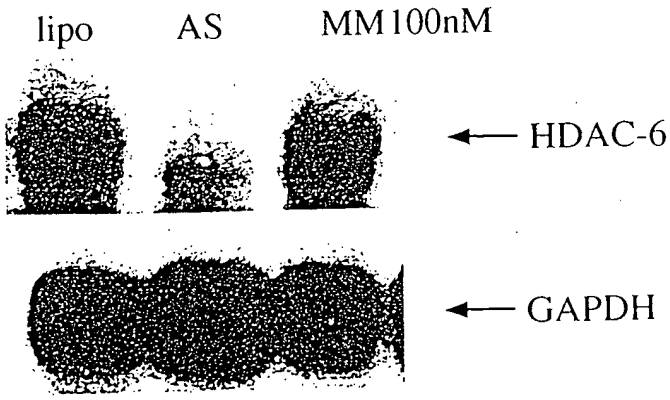


FIG. ~~9C~~ 1C

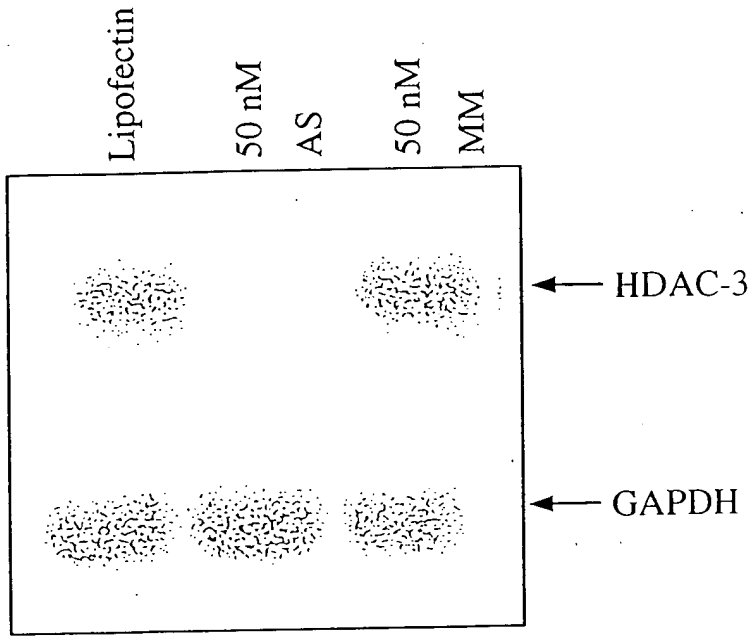


FIG. ~~9D~~ 1D

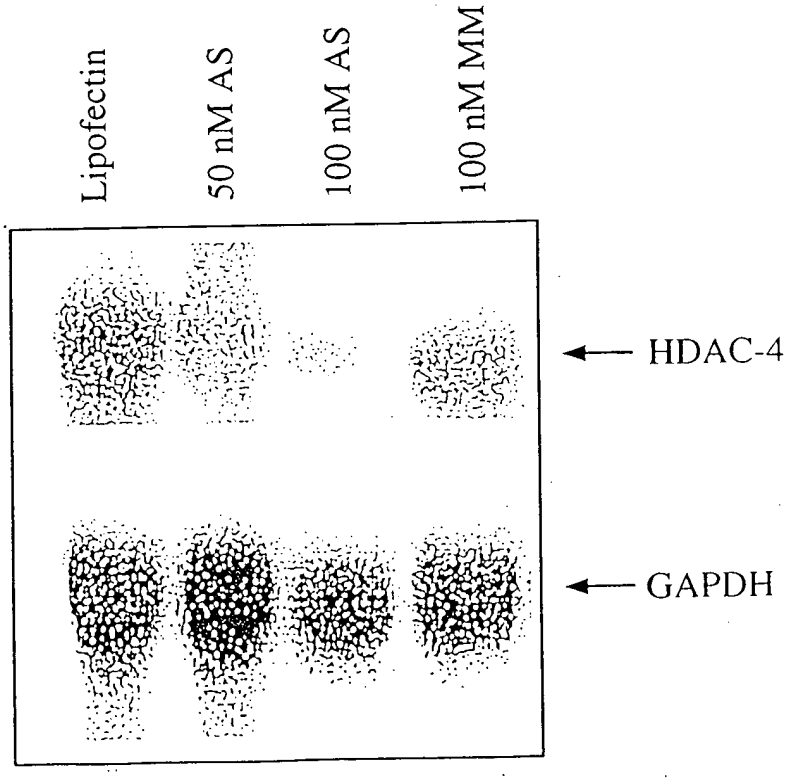


FIG. ~~9E~~ 1E

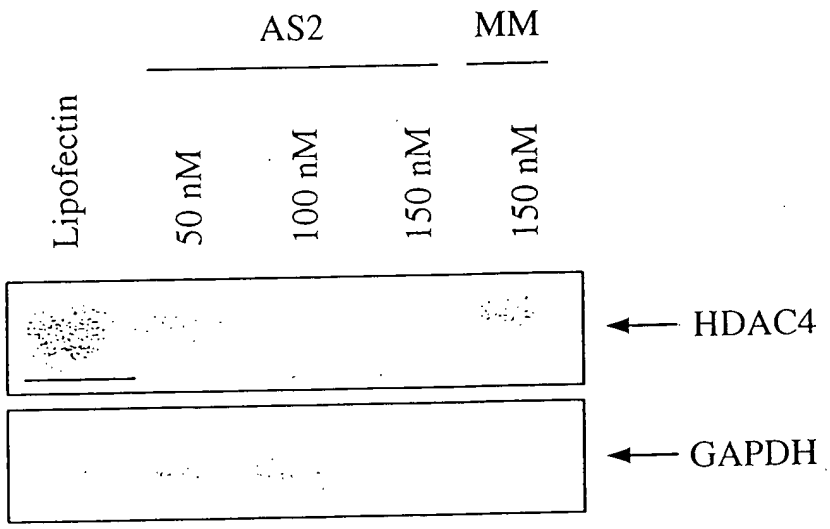


FIG. ~~9F~~ 1F

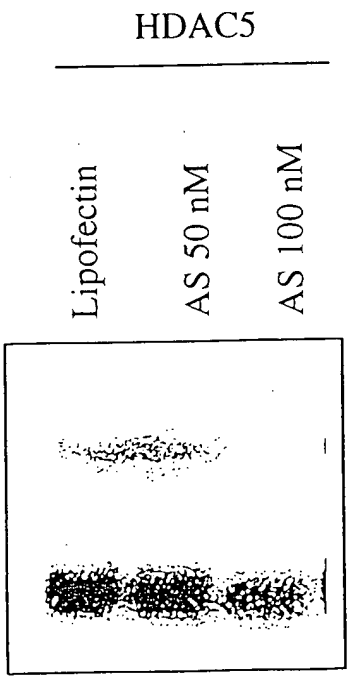


FIG. ~~9G~~ 1G

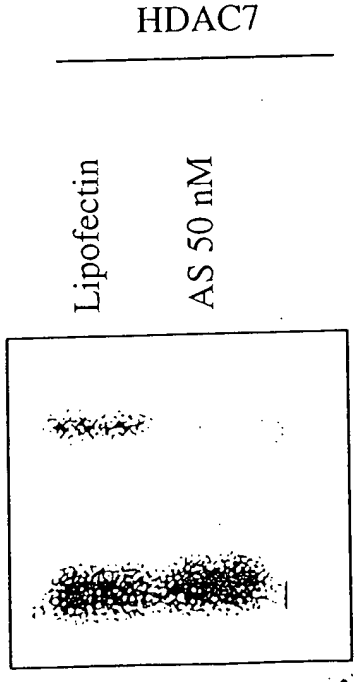


FIG. ~~9H~~ 1H

~~28/37~~ 4/13

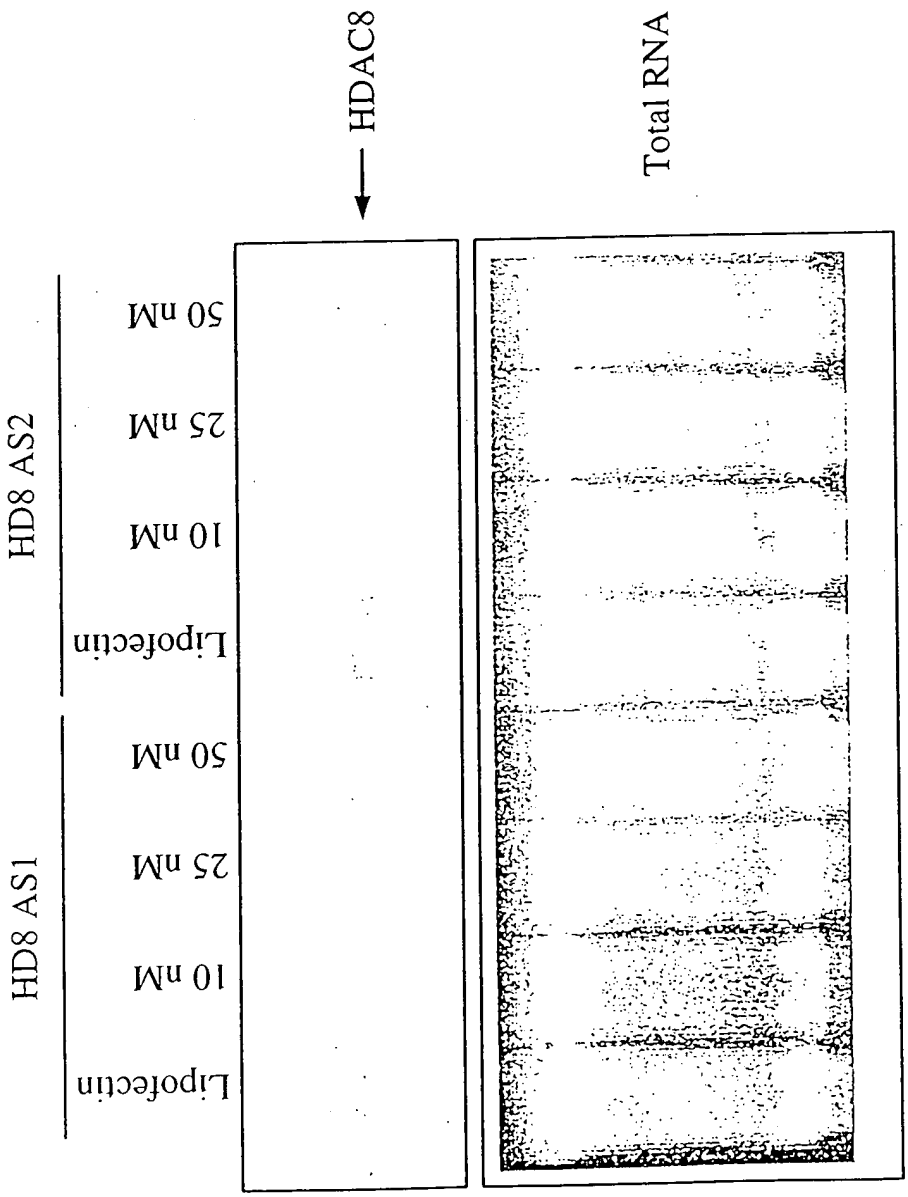
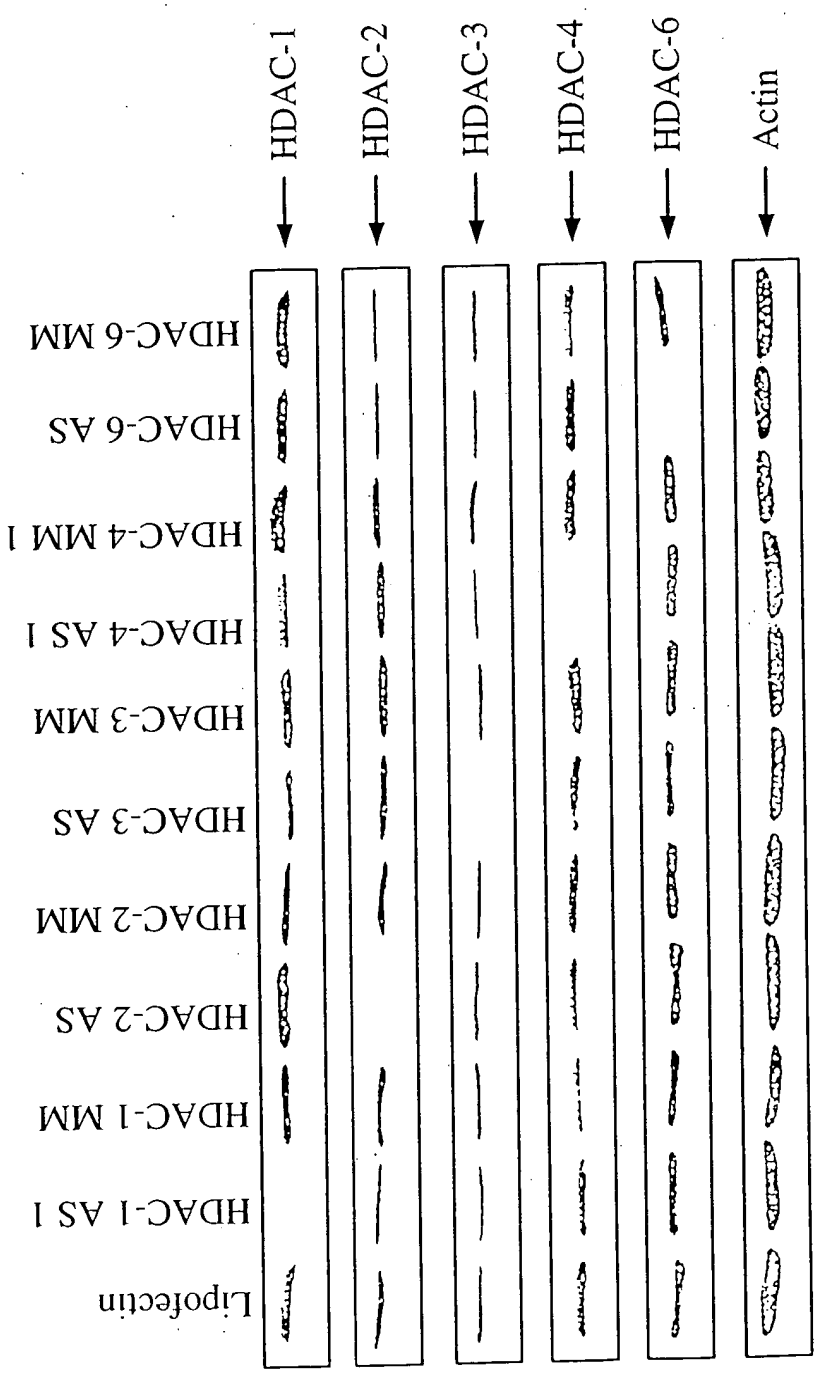


FIG. 1I



AS = Antisense
MM = Mismatch
NS = Non-specific control
3 day treatment
Oligonucleotide cone – 50nM

FIG. ~~10A~~ 2A

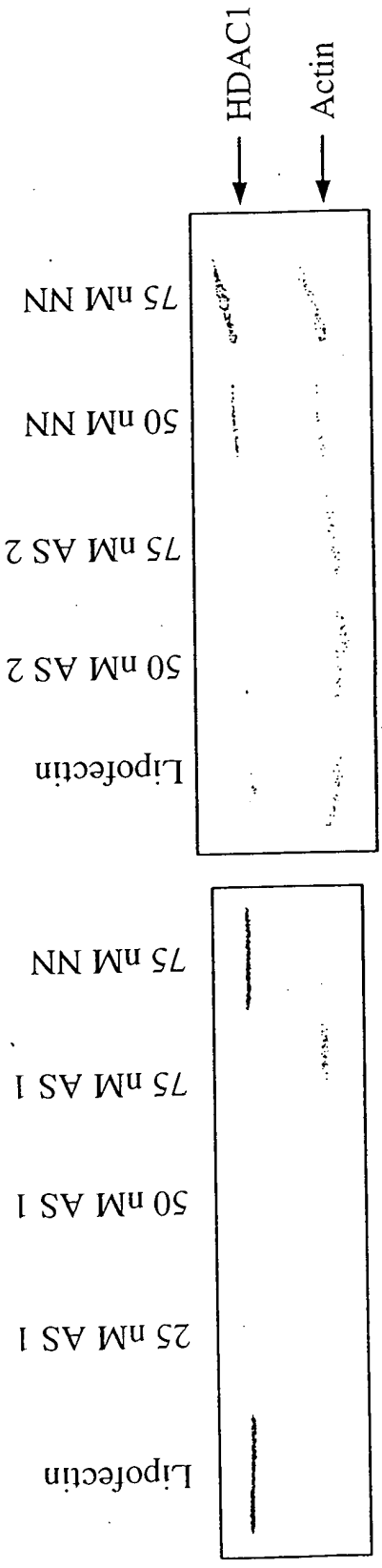

HDAC1
Actin
Lipofectin
50 nM AS 2
75 nM AS 2
50 nM NN
75 nM NN
Lipofectin
25 nM AS 1
50 nM AS 1
75 nM AS 1
75 nM NN

FIG. ~~10B~~ 2B

ANNOTATED MARKED-UP DRAWINGS

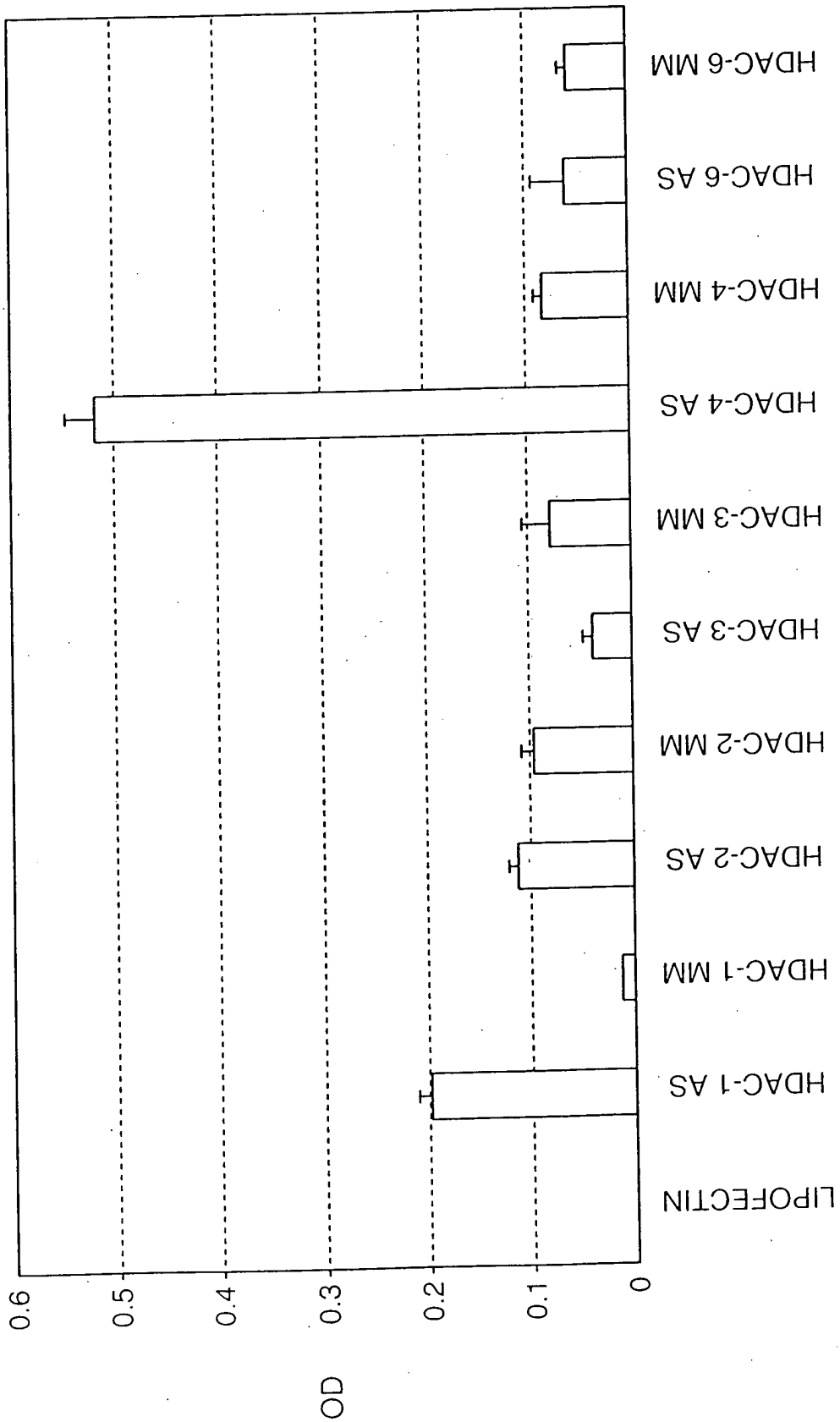


FIG. 13

~~32/37~~ 8/13

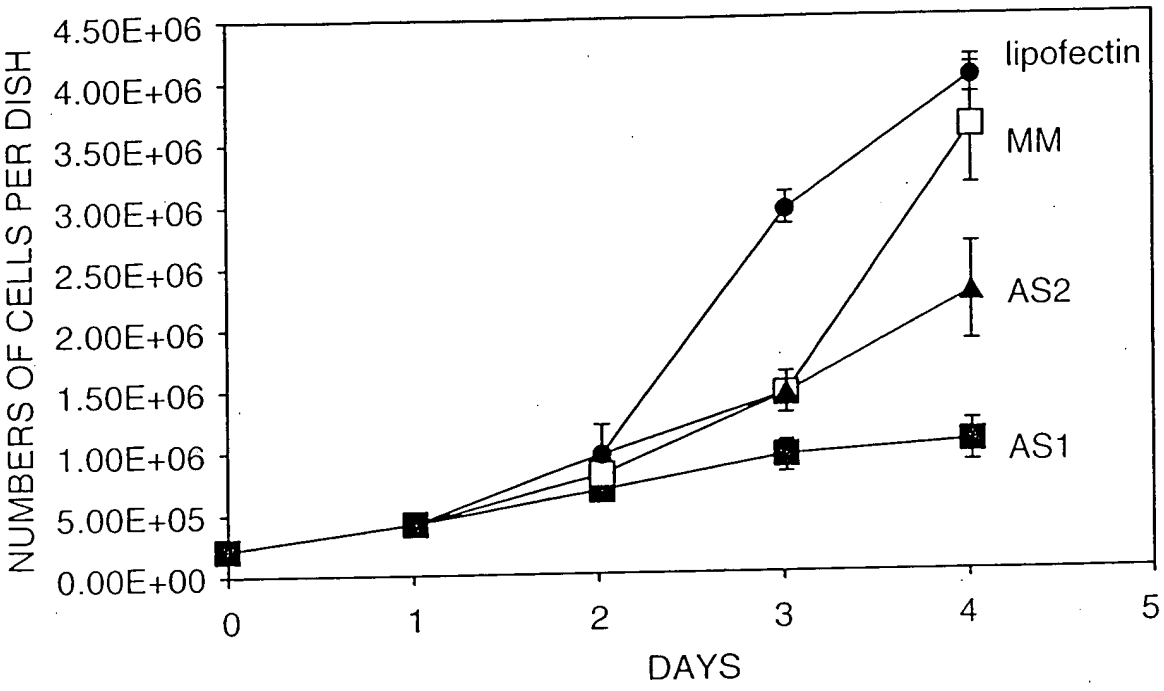


FIG. ~~12A~~ 4A

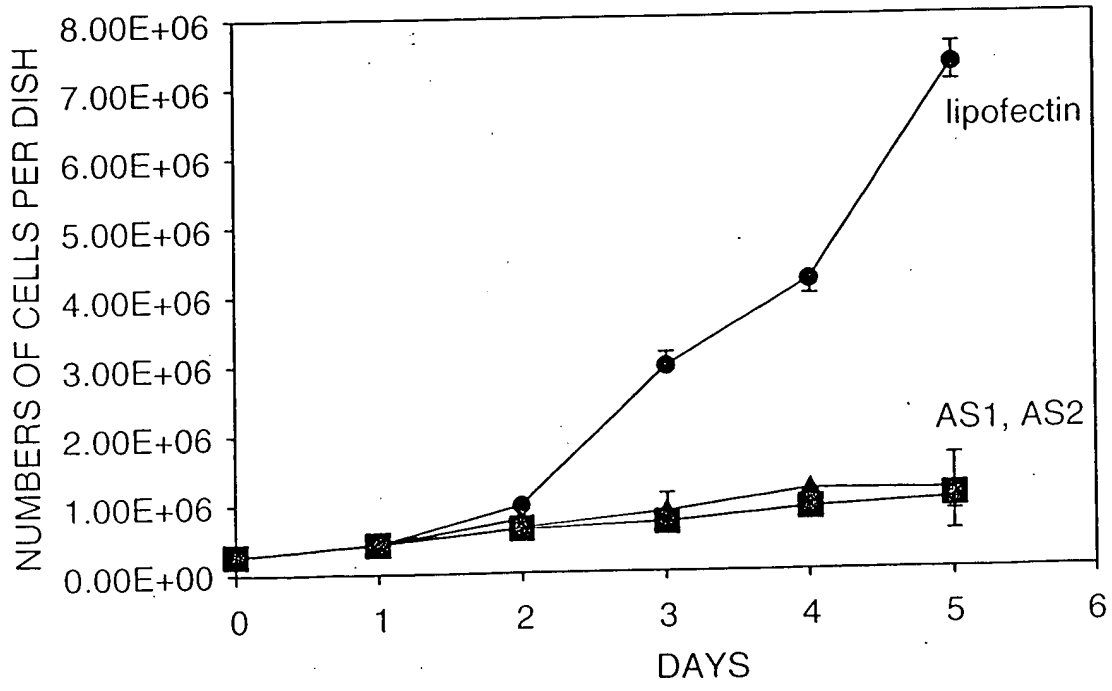


FIG. ~~12B~~ 4B

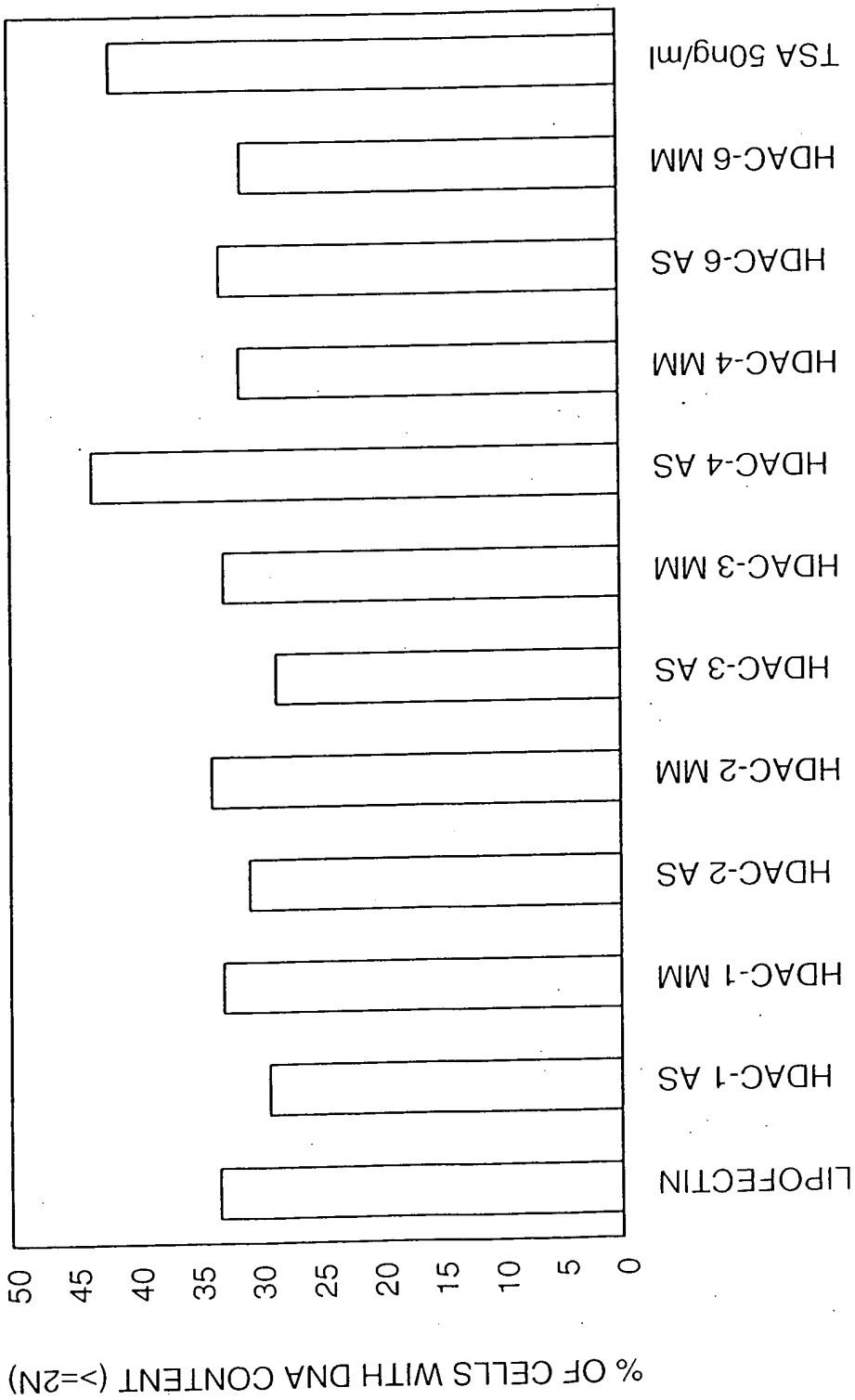

% OF CELLS WITH DNA CONTENT (>=2N)
0
5
10
15
20
25
30
35
40
45
50
LIPOFECTIN
HDAC-1 AS
HDAC-1 MM
HDAC-2 AS
HDAC-2 MM
HDAC-3 AS
HDAC-3 MM
HDAC-4 AS
HDAC-4 MM
HDAC-6 AS
HDAC-6 MM
TSA 50ng/ml

FIG. 13-5

~~94/37~~ 10/13

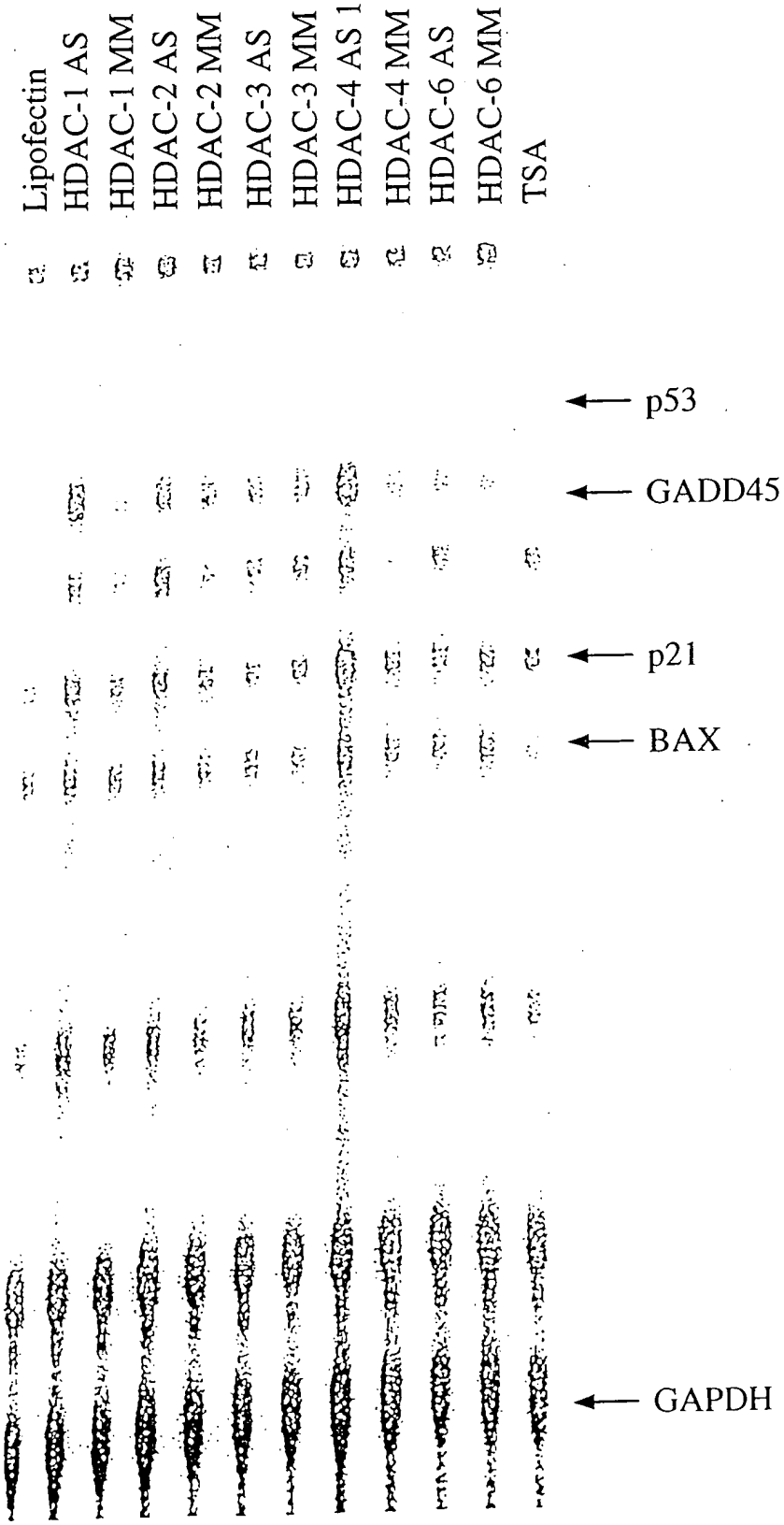


FIG. ~~14~~ 6

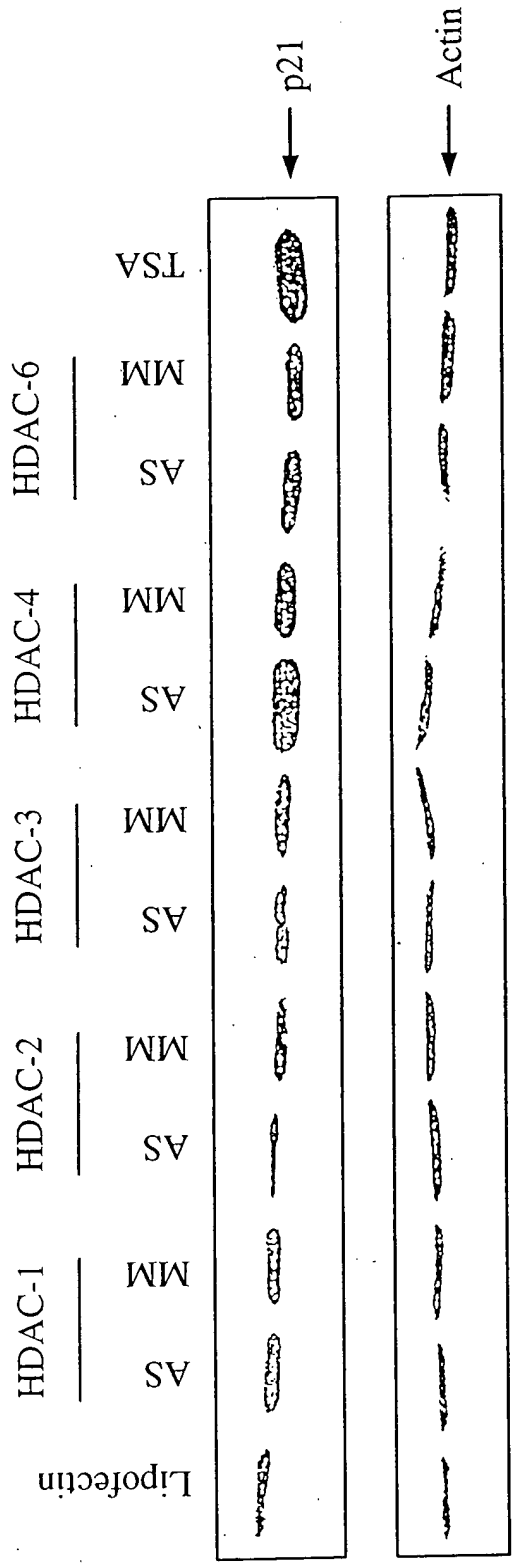

p21
Actin
Lipofectin
HDAC-1
AS
MM
HDAC-2
AS
MM
HDAC-3
AS
MM
HDAC-4
AS
MM
HDAC-6
AS
MM
TSA

FIG. ~~15~~ 7

ANNOTATED MARKED-UP DRAWINGS

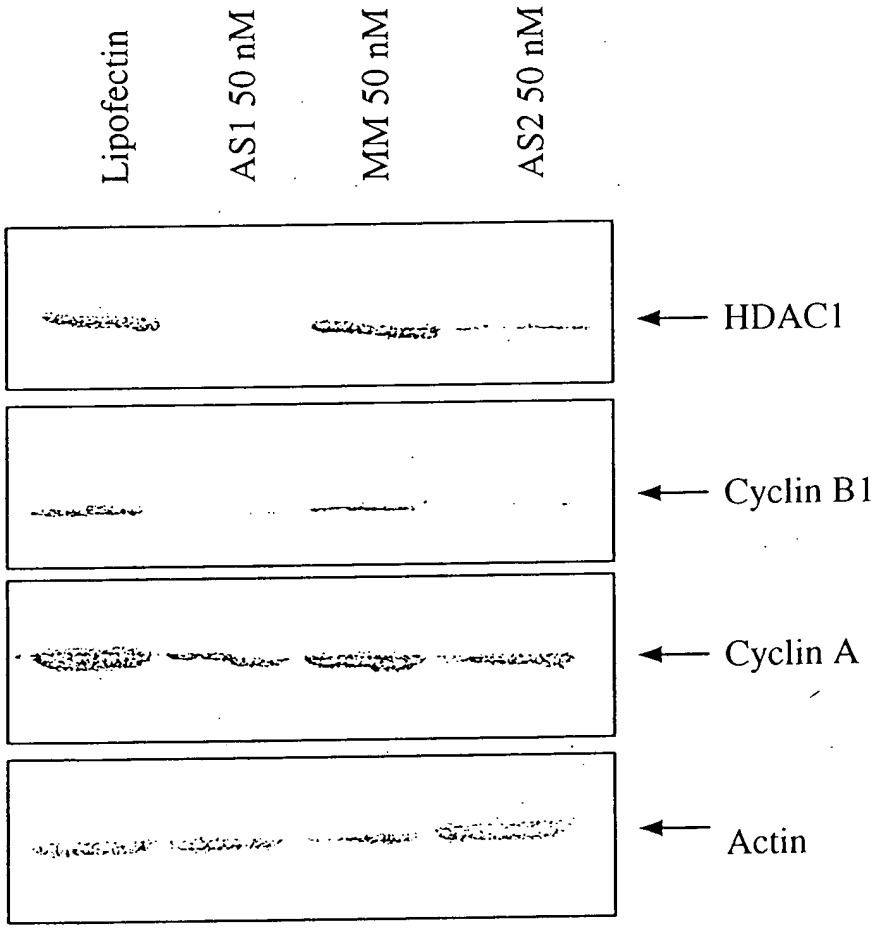


FIG. ~~16~~ 8

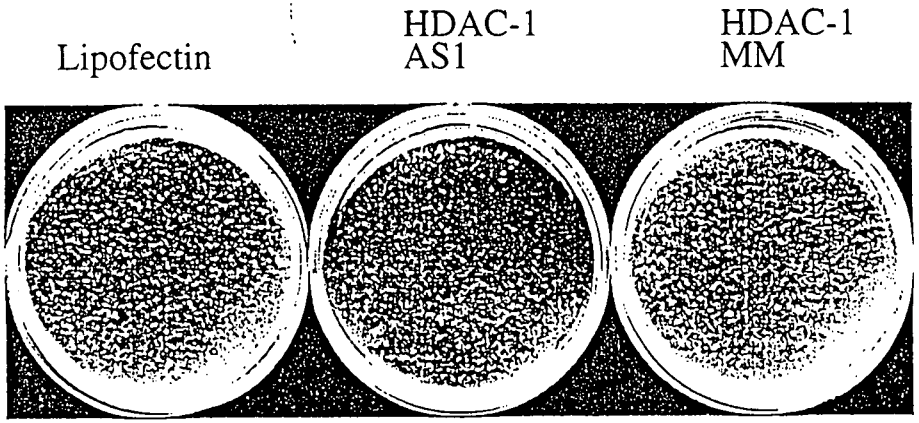


FIG. ~~17A~~ 9A

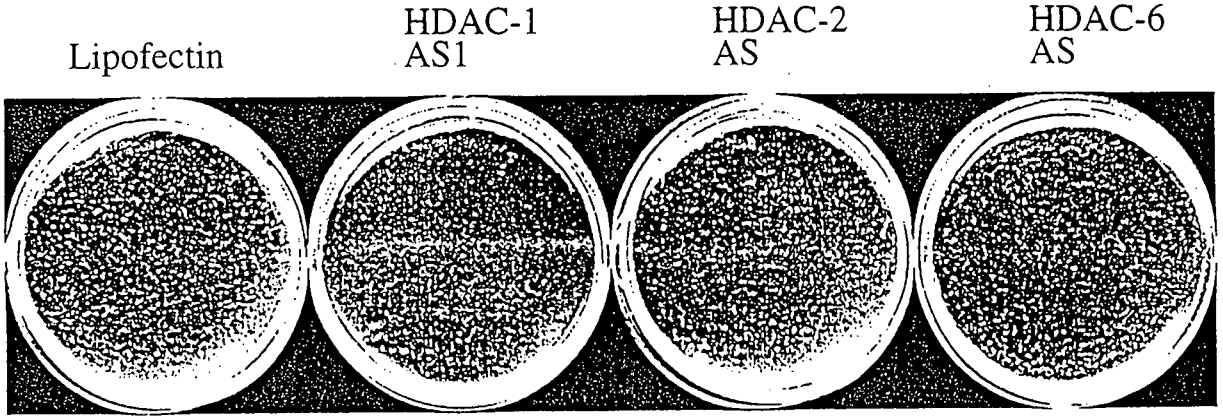


FIG. ~~17B~~ 9B

~~37/37~~ 13/13

ANNOTATED MARKED-UP DRAWINGS